Computer-aided diagnosis

Why CAD?

Even with excellent image quality, diagnostic performance by humans is variable and may be affected by many internal and external factors:

- Experience
- Distraction
- Satisfaction of search
- Fatigue
- Psychophysical limitations of the eye-brain system e.g. estimating ratios of volumes is not linear.

CAD applications in radiology

- Mammography
  - Density measurement
  - Clustered microcalcification detection and classification
  - Mass detection and classification
  - Analysis of parenchymal patterns for assessing cancer risk
- Chest
  - Lung nodule detection in Xray and CT
  - Interstitial infiltrate detection
  - Pneumothorax detection
  - Automated analysis of heart sizes
- Gastrointestinal
  - Detection of polyps in virtual colonoscopy
- Skeletal
  - Automated estimation/detection of osteoporosis

Detection and classification of breast lesions

- What are our goals?
- Methods for detecting microcalcifications
- Methods for detecting masses
- Using features to classify microcalcifications
- Using features to classify masses
- Effect of CAD on radiologists' diagnostic performance

Goals of CAD of breast lesions

Increased sensitivity of detecting lesions

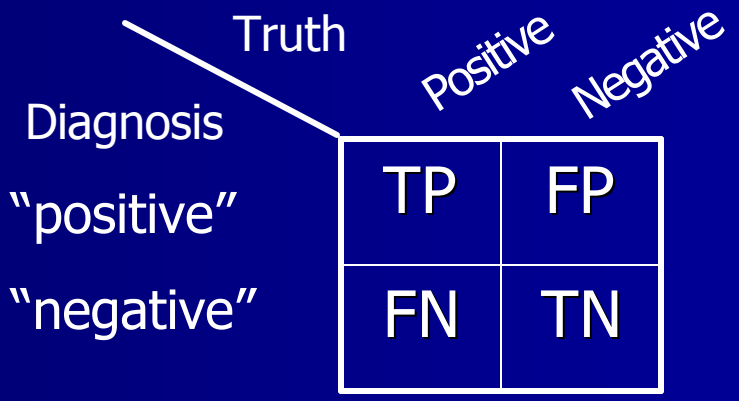
- Sensitivity is often high (85-95%), but a "second read" by another radiologist has been shown to increase sensitivity by as much as 15%

Improved classification – i.e., reduce biopsies of benign lesions and increase biopsies of malignant lesions

- Fraction of lesions proven malignant at biopsy is only 15% to 30%

Diagnostic performance metrics

Truth table ✍



Sensitivity = TP / (TP + FN)

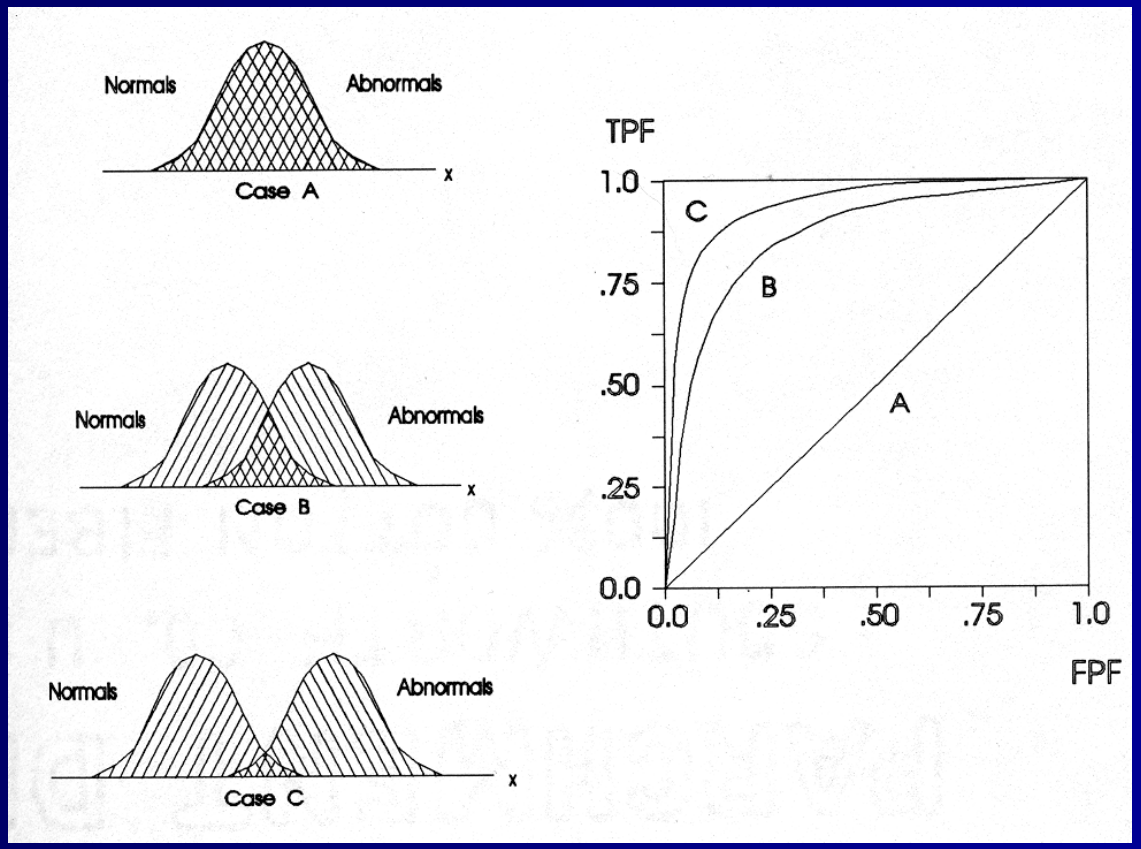
Specificity = TN / (TN + FP)

Accuracy = (TP + TN) / (all cases

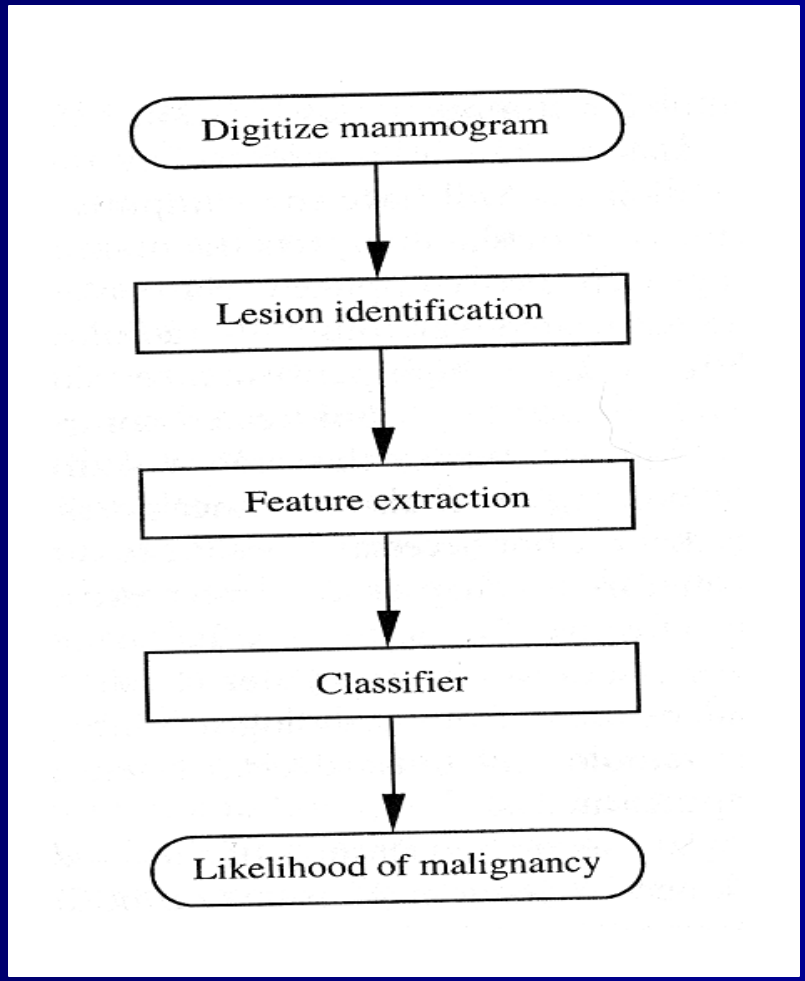
"Diagnostic performance" is seldom just "accuracy"

Diagnostic performance metrics

Area under the ROC curve (A_z) is a common metric.



Typical CAD processing steps



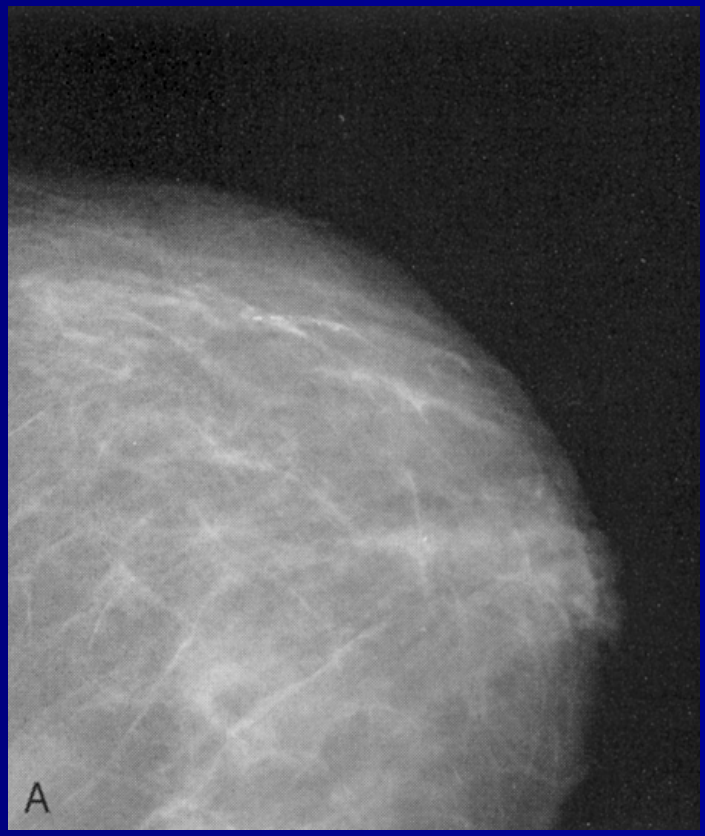
Detecting microcalcifications

Microcalcifications are calcium deposits as small as 0.1-0.3 mm in diameter. Pleomorphic, curvilinear or branched shapes are usually found with malignant lesions. Pearl-like appearances are associated with benign processes.

Clusters of 3 or more within a square centimeter are considered suspicious. 30-50% of cancers contain such clusters of microcalcifications.

Detecting microcalcifications

Detail of mammogram showing a focus of microcalcifications.



Detecting microcalcifications

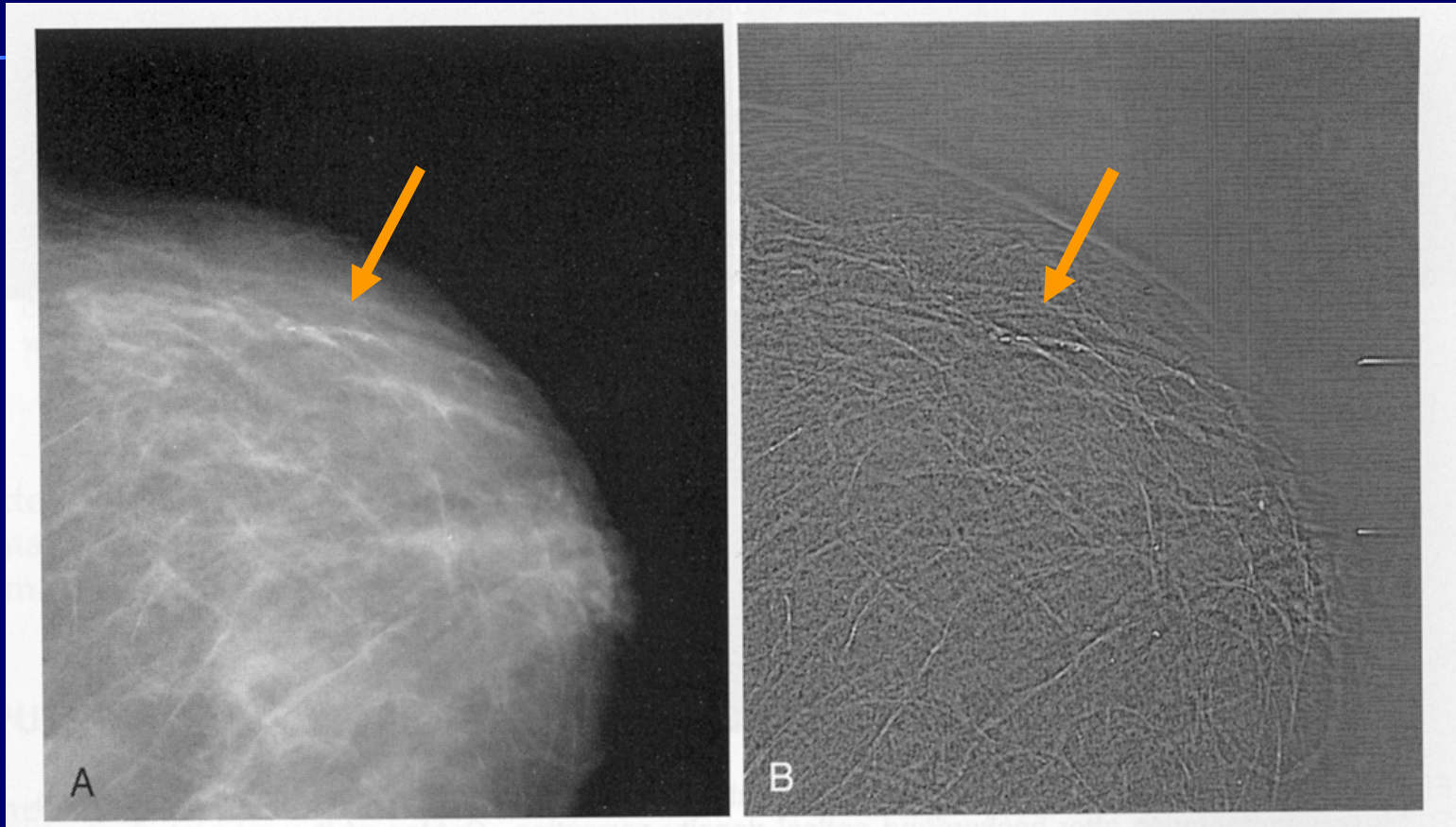


Figure 2. Example of a technique in computer vision. *A*, Detail of a mammogram showing a focus of microcalcifications. *B*, Processed image in which image features having the spatial dimensions of microcalcifications are emphasized. The image in *B* is obtained by subtracting slightly sharpened and slightly blurred versions of the original image.

Detecting microcalcifications

One detection approach:

- Find bright, almost circular spots
- Estimate size D and local contrast C
- Mark a spot as a microcalcification if $C > C_T(D)$, where $C_T(D)$ is a threshold varying with size.

Scale-space signatures for the detection of clustered microcalcifications in digital mammograms. T. Netch & H.-O. Peitgen, IEEE Transactions on Medical Imaging. 18(9):774-786

Detecting microcalcifications

Scale-space method of finding spots:

- Bright spots correspond to local maxima in Laplacian-convolved images if the kernel size is chosen appropriately.
- To detect different sizes, use different kernels.

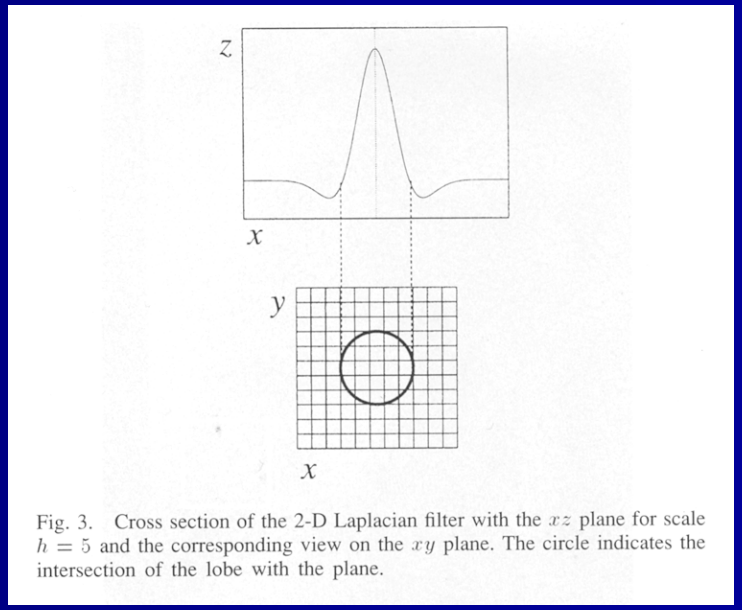


Fig. 3. Cross section of the 2-D Laplacian filter with the xz plane for scale $h = 5$ and the corresponding view on the xy plane. The circle indicates the intersection of the lobe with the plane.

Detecting microcalcifications

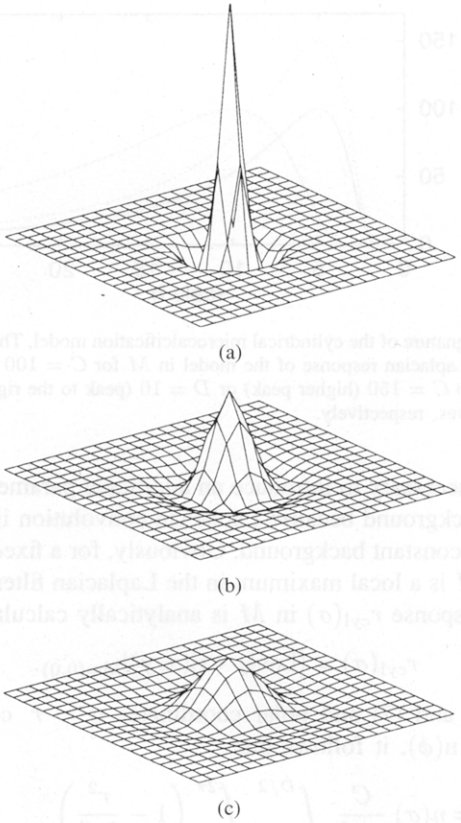


Fig. 4. Examples of normalized Laplacian filter kernels for scales (a) $h = 3$, (b) $h = 5$, and (c) $h = 7$.

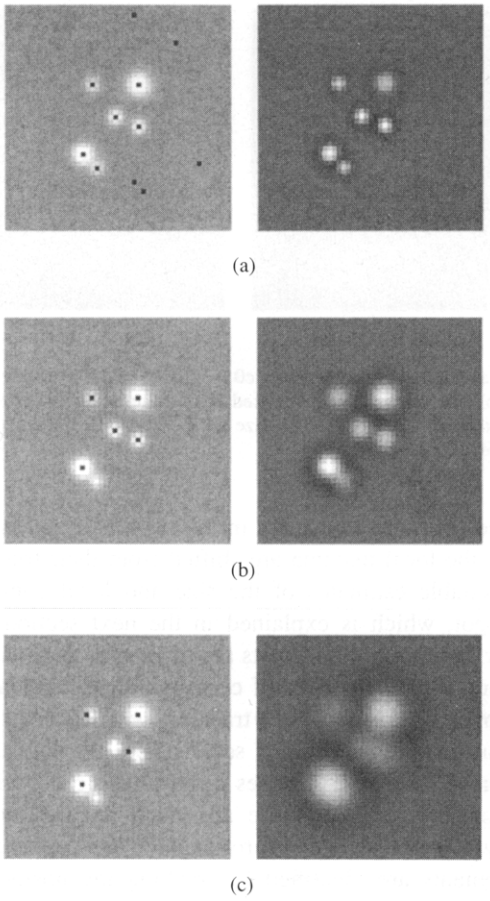


Fig. 5. Artificial image consisting of bright spots of different size and local contrast. As well, Gaussian noise with zero mean and fixed standard deviation is added. In the left row the black pixels mark the location of local maxima of the Laplacian filtered image for scales (a) $h = 2$, (b) $h = 5$, and (c) $h = 10$. The corresponding filtered images are shown at the right.

Detecting microcalcifications

Scale-space method of finding spots:

- Tracking the position of local maxima of each candidate pixel through scale-space enables the true center of the spot to be found at the maximum value along the path.
- Accurate centering is important for further measurements that attempt to select the best microcalcification candidates.

Minimizing false-positive reports is vital to acceptance of CAD as a "second read".

Detecting microcalcifications

Microcalcification "signature"

- Model as a cylinder of diameter D and height C
- Signature as a function of scale is defined as:

$$r_{\mathrm{cyl}}(h) = C\, e\, \frac{D^2}{h^2}\, e^{-(D^2/h^2)}.$$

Signature curves

D = h @ max[r]

C = max[r]

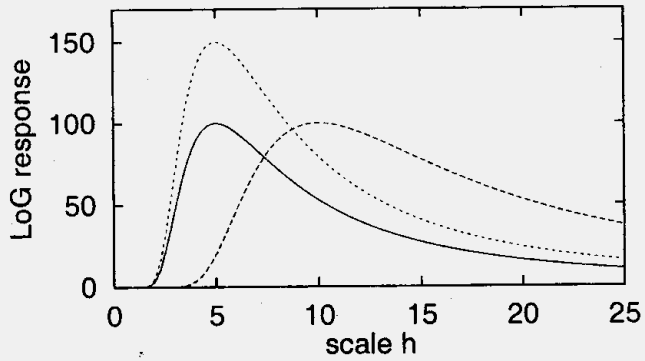


Fig. 7. Signature of the cylindrical microcalcification model. The solid curve shows the Laplacian response of the model in M for $C = 100$ and $D = 5$. A change to $C = 150$ (higher peak) or $D = 10$ (peak to the right) yield the dashed curves, respectively.

Detecting microcalcifications

Using microcalcification signatures:

Measured signature is response in scale-space along path; D and C are estimated from that signature.

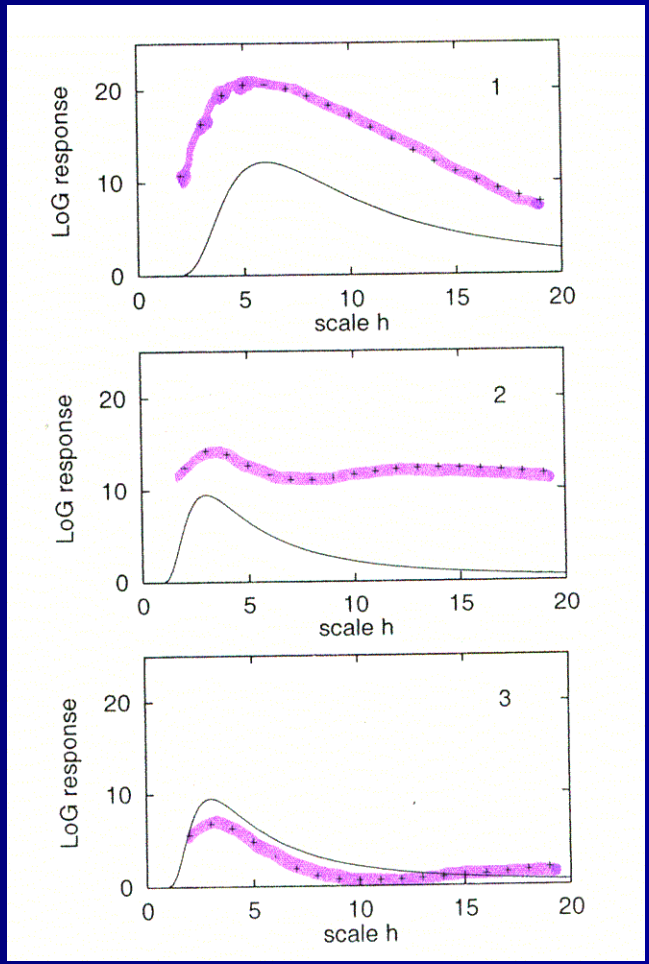
Comparing the measured signature to model signature for the same size and a C threshold selects which microcalcifications to keep.

Detecting microcalcifications

Measured signal exceeds model – keep it.

Measured signal exceeds model – keep it.

Measured signal less than model – discard it.



Detecting microcalcifications

Mark a spot as a microcalcification if $C > C_T(D)$. $C_T(D)$ is adjusted to control the detection sensitivity of the algorithm.

Using a set of mammograms with known truth about number and location of microcalcifications enables "training" the threshold function to achieve a desired sensitivity or specificity.

At 0.5 false-positives per image, the true-positive fraction reported by these authors is about 0.9.

Detecting masses

Unlike calcifications, many characteristics of masses can be simulated by normal tissue.

Detection schemes need to rely on features such as:

- Circumscribed configurations
- Asymmetry compared to the other breast
- Local textural changes
- Radiating patterns of density

Detecting masses

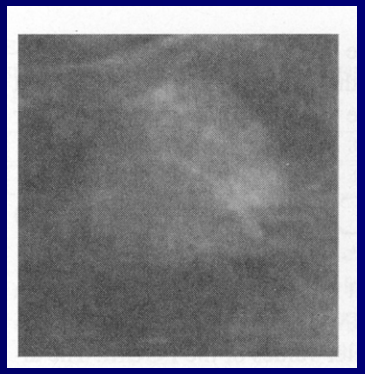
One detection approach:

- Uses morphological operations to emphasize masses.
- An opening operation using a structuring element smaller than the size of masses
- Subtraction of the original image (the combination of the two is sometimes called a "tophat" operation)
- A second tophat operation with a large kernel
- Result is step 2 – step1.

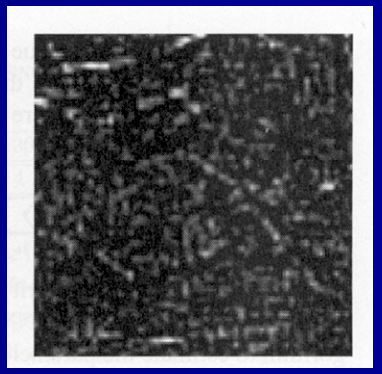
H Li, Y Wang, KJ Ray Liu, S-CB Lo, M Freedman. Computerized radiographic mass detection – part I: lesion site selection by morphological enhancement and contextual segmentation. IEEE Transactions on Medical Imaging 20(4):289-301

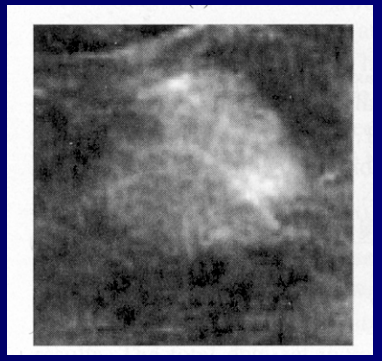
Detecting masses

f(i,j) = image

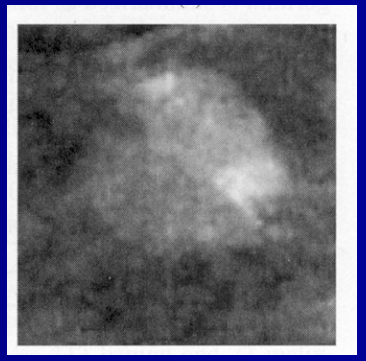


r1(i,j)= max[0, f(i,j) – (f **o** B1)(i,j)]





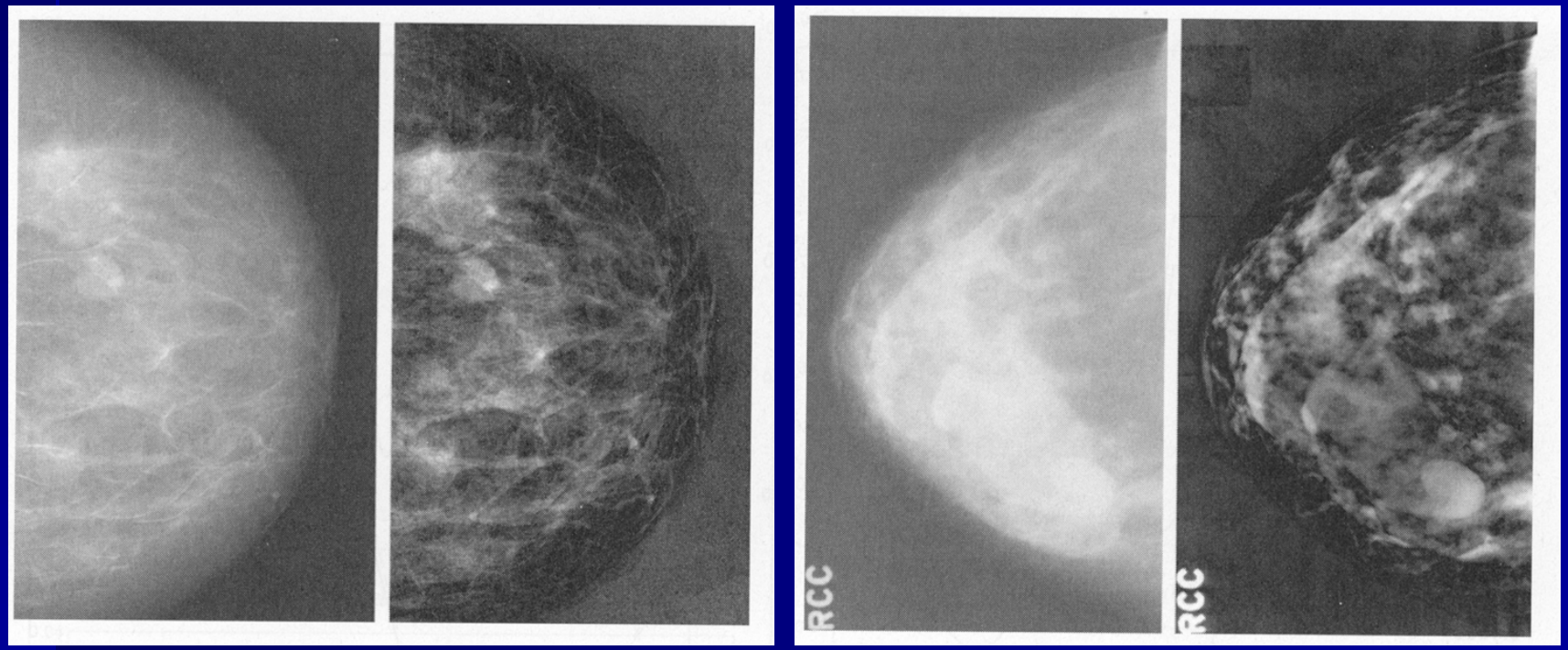
r2(i,j)= max[0, f(i,j) – (f **o** B2)(i,j)



result= max[0, r2(i,j) – r1(i,j)]

Detecting masses

Original and mass-enhanced mammograms.



Detecting masses

Contextual Bayesian relaxation labeling (CBRL)

YUCK!

$$p(x_i|\mathbf{l}_{\partial i}) = \sum_{k=1}^{K} \pi_k^{(i)} p_k(x_i) \qquad \pi_k^{(i)} = p(l_i = k|\mathbf{l}_{\partial i}) = \frac{1}{m^2 - 1} \sum_{j \in \partial i,\, j \neq i} I(k, l_j)$$

$$p_k(x_i) = \frac{\alpha \beta_k}{2\Gamma(1/\alpha)} \exp[-|\beta_k(x_i - \mu_k)|^{\alpha}], \qquad \alpha > 0,$$

$$\beta_k = \frac{1}{\sigma_k} \left[\frac{\Gamma(3/\alpha)}{\Gamma(1/\alpha)}\right]^{1/2}.$$

where μ_k is the mean, $\Gamma(\cdot)$ is the Gamma function. β_k is a parameter related to the variance σ_k.

local neighborhood (m x m)

Gaussian probability density function on grey levels

m x m compatibility matrix where label matches k, = 1

Detecting masses

Labeled image, pass 0

Selects the most likely label

When the labeling is unchanged by dilation, it is stable.

CBRL Algorithm:

1) Given $\mathbf{l}^{(0)}$, $m = 0$
2) Update pixel labels
   - Randomly visit each pixel for $i = 1, \ldots, N_1 N_2$
   - Update its label l_i according to

$$l_i^{(m)} = \arg\left\{ \max_k \pi_k^{(i)(m)} p_k(x_i) \right\}.$$

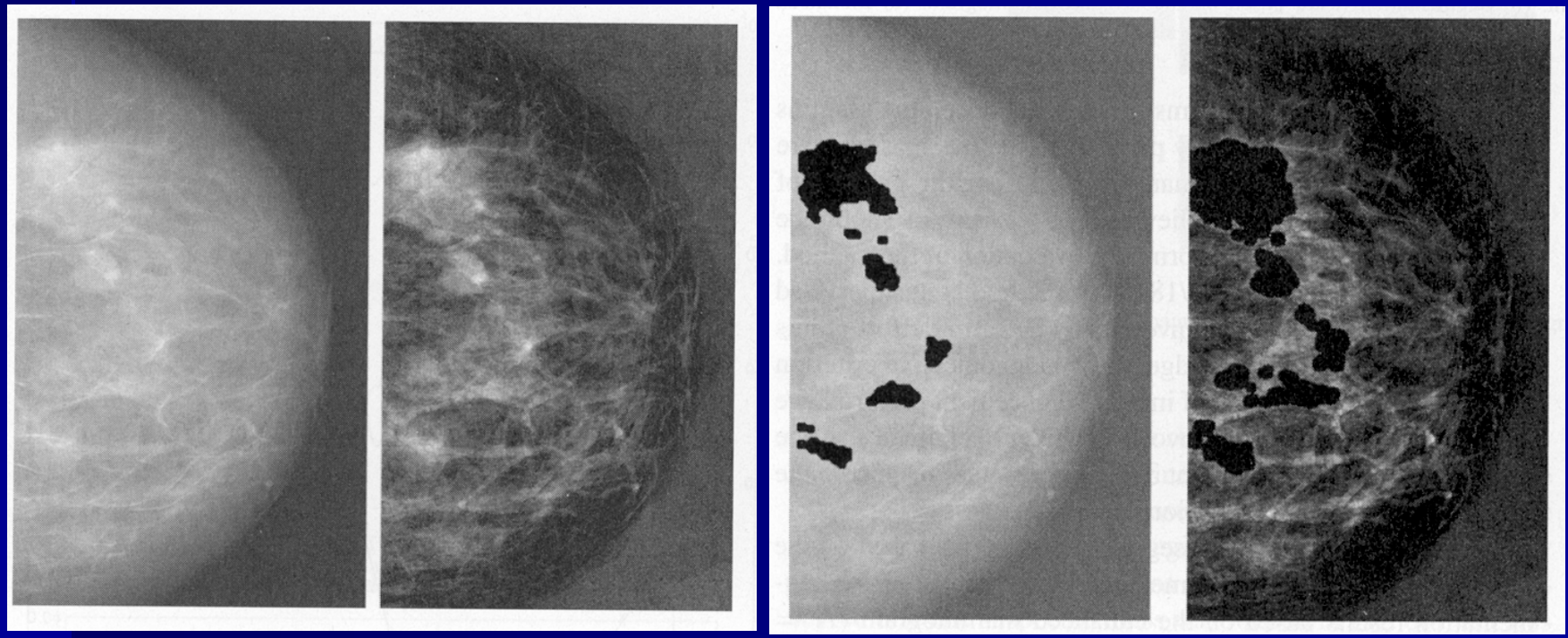
3) When

$$\frac{\sum (\mathbf{l}^{(m+1)} \oplus \mathbf{l}^{(m)})}{N_1 N_2} \leq 1\%,$$

stop; otherwise, $m = m + 1$, and repeat Step 2.

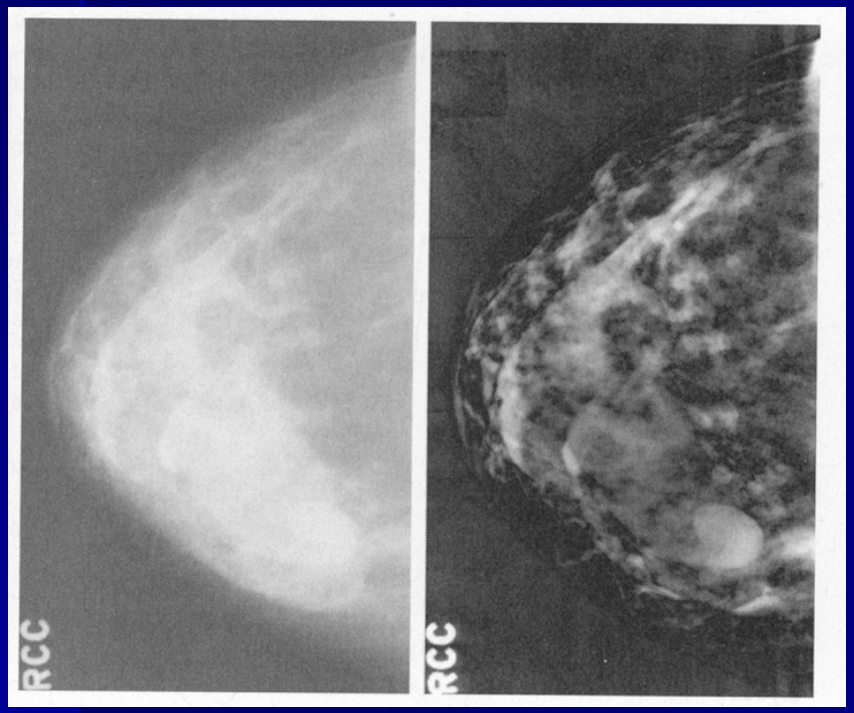
Detecting masses

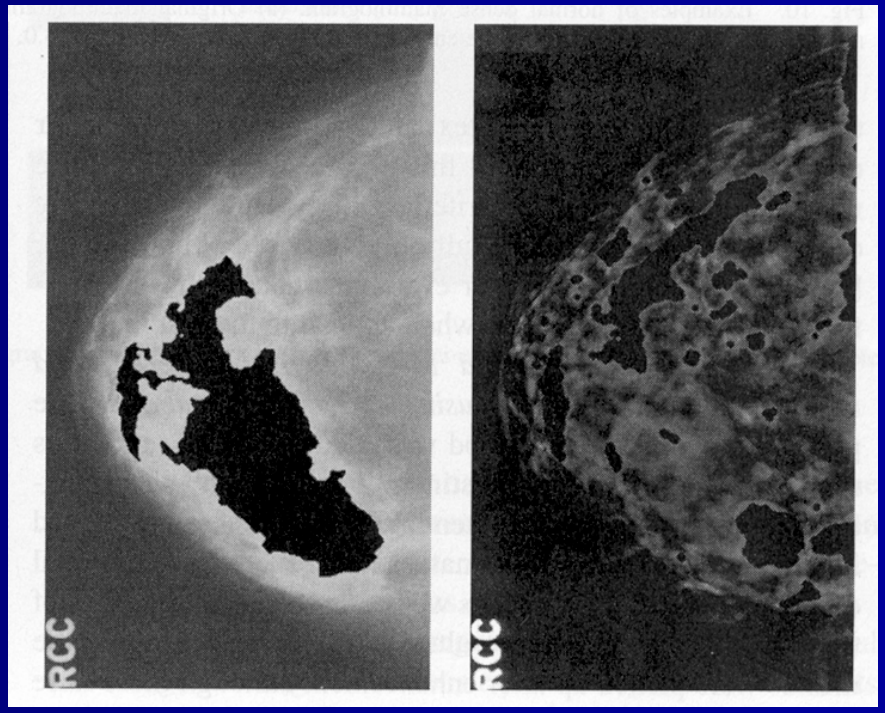
Mass segmentation using CBRL on original and enhanced images



Detecting masses

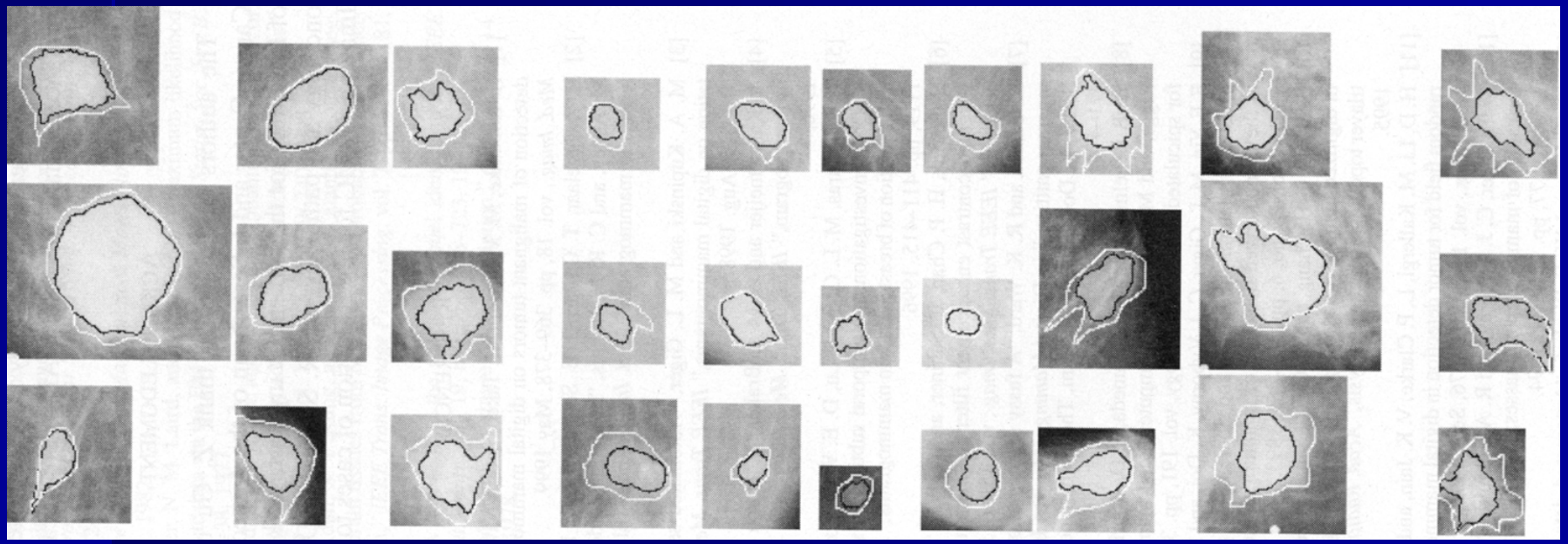
Mass segmentation using CBRL on original and enhanced images





Detecting masses

Mass segmentation. Black lines are from CBRL, white from radiologists. Authors reported 0.97 sensitivity, with many false-positives, and rely on classification techniques to reduce FPs.



Important lesion features

Extensive interviews with radiologists attempted to capture essential features that influence their classification of lesions as benign or malignant.

The earliest CAD approach was presenting a checklist of features to the radiologist and requiring a score of each feature. The computer aid was simply a prediction of malignancy based on the feature scores. It worked – lesion classification improved from 0.83 to 0.88 (A_z).

Important lesion features – what the radiologists say

Mass size: CC view
Mass size: lateral view
Mass shape
Mass spiculation
Mass invasion
Mass singleness
Homogeneity of soft tissue
Number of calcification elements
Size of calcification cluster: CC view
Size of calcification cluster: lateral view
Smoothness of typical calcification element
Evidence of architectural distortion
Evidence of nipple or skin retraction

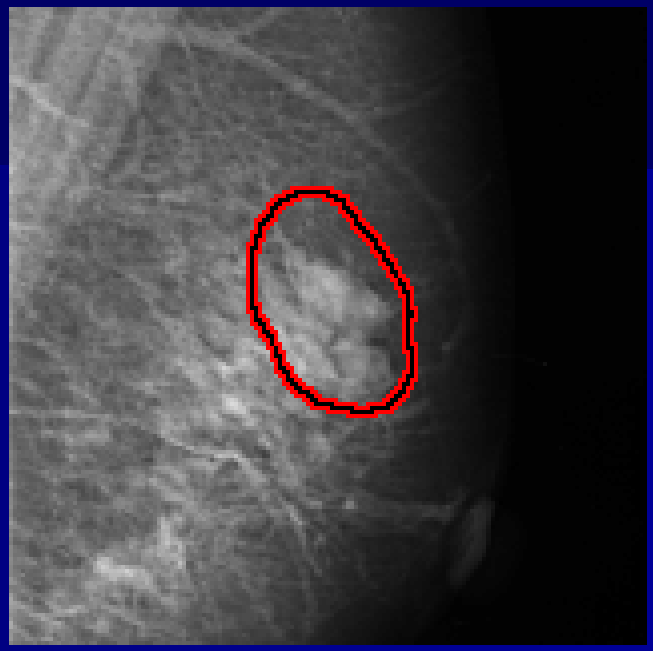
Getty Dj, Pickett Rm, D'Orsi CJ, Swets JA. Enhanced interpretation of diagnostic images. **Investigative Radiology** 1988; 23:240-252.

Lesion features

L MLO view

Lesion type: Mass; oval; circumscribed

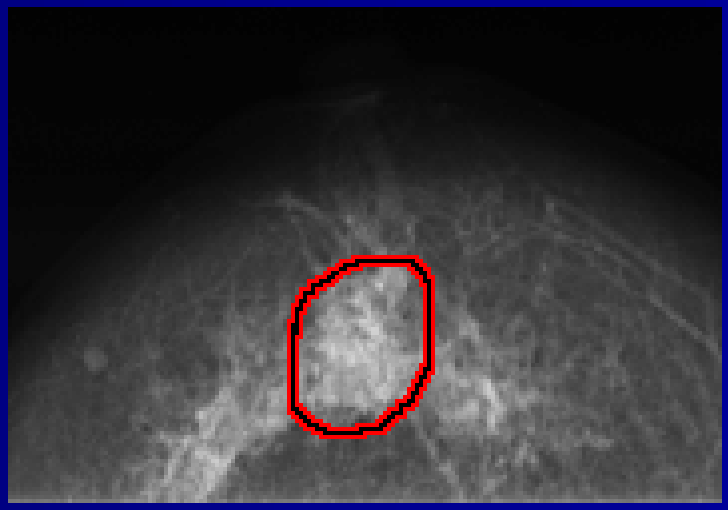
Pathology: benign



L CC view

Lesion type: Mass; irregular; ill-defined

Pathology: benign



Cases obtained from University of South Florida, Digital Database for Screening Mammography (DDSM).

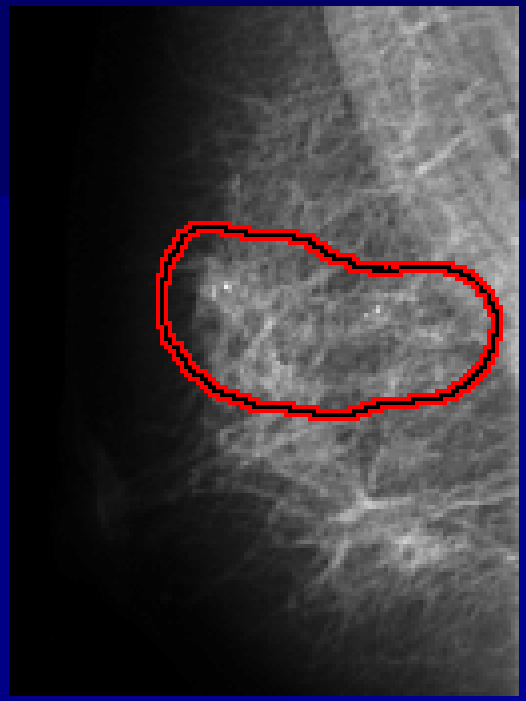
Lesion features

R MLO view

Lesion type: Calcification; pleomorphic; segmental

Lesion type: Mass; irregular; ill-defined

Pathology: malignant

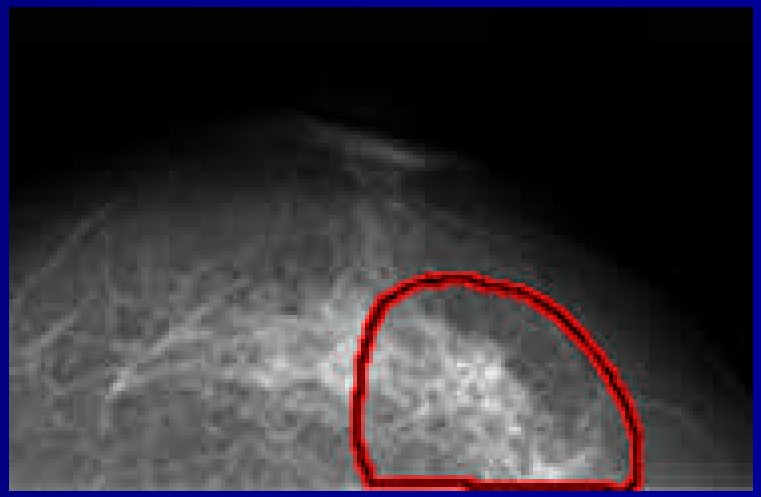


R CC view

Lesion type: Calcification; pleomorphic; segmental

Lesion type: Mass; irregular; spiculated

Pathology: malignant



Feature-based classification - calcifications

Computer-extracted features:

- Cluster circularity
- Cluster area
- Number of microcalcifications
- Average effective volume of microcalcifications
- Relative standard deviation in effective thickness
- Relative standard deviation in effective volume
- Average area of microcalcifications
- 2nd highest microcalcification-shape-irregularity in a cluster

Jiang Y, Nishikawa RM, Schmidt RA, Metz CE, Giger ML, Doi K. Improving breast cancer diagnosis with computer-aided diagnosis. **Academic Radiology** 1999;6:22-33.

Feature-based classification - masses

Computer-extracted features:

- Spiculation
- Margin sharpness
- Average grey level
- Texture measure

Huo Z, Giger ML, Vyborny CJ, Wolverton DE, Schmidt RA, Doi K. Automated computerized classification of malignant and benign masses on digitized mammograms. **Academic Radiology** 1998; 5:155-168..

Feature-based classifiers

- Linear discriminant analysis (LDA) – feature space clustering.
- Artificial neural network (ANN) that is trained with feature measurements from a set of mammograms with known truth and tested on another proven dataset. ANN output is transformed to a probability of malignancy.

CAD and diagnostic performance

In mammography the ultimate result of an detecting something in an examination is a recommendation of:

- Routine follow-up
- Short-term follow-up
- Alternative biopsy (needle biopsy)
- Surgical biopsy

CAD and diagnostic performance

TABLE 2 Attending radiologists' assessments of likelihood of malignancy and their clinical recommendations on a malignant case with computer-assessed likelihood of malignancy of 60%[a]

Attending radiologists	Assessments of suspicion		Clinical recommendations	
	Unaided	CAD	Unaided	CAD
A	53%	84%	Alternative biopsy	Surgical biopsy
B	25%	50%	Short-term follow-up	Surgical biopsy
C	55%	58%	Alternative biopsy	Alternative biopsy
D	10%	49%	Routine follow-up	Alternative biopsy
E	55%	66%	Surgical biopsy	Surgical biopsy

[a] Reprinted from [59] with permission.

TABLE 3 Attending radiologists' assessments of likelihood of malignancy and their clinical recommendations on a benign case with computer-assessed likelihood of malignancy of 13%[a]

Attending radiologists	Assessments of suspicion		Clinical recommendations	
	Unaided	CAD	Unaided	CAD
A	51%	14%	Alternative biopsy	Short-term follow-up
B	54%	20%	Surgical biopsy	Short-term follow-up
C	56%	13%	Alternative biopsy	Routine follow-up
D	60%	53%	Alternative biopsy	Short-term follow-up
E	42%	15%	Surgical biopsy	Short-term follow-up

[a] Reprinted from [59] with permission.

CAD and diagnostic performance

Results of a very effective computerized classifier. Note that it performs significantly better than did unaided radiologists (Az = 0.80 and 0.62).

Even when the aid (a probability of malignancy) was available, radiologists' performance did not reach computers' (Az = 0.76).

Why?

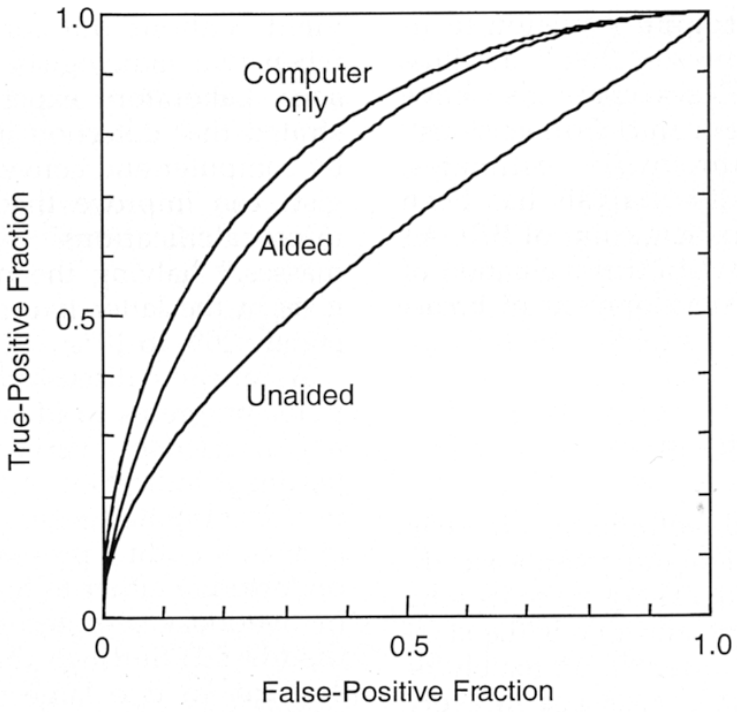


Figure 12. Performance of radiologists and computer in characterizing microcalcifications as malignant or benign as plotted on an ROC curve. Radiologists given the computer information outperformed unaided radiologists. (*From* Jiang Y, Nishikawa RM, Schmidt RA, et al: Improving breast cancer diagnosis with computer-aided diagnosis. Academic Radiology 6:22, 1999; with permission.)

CAD workstation

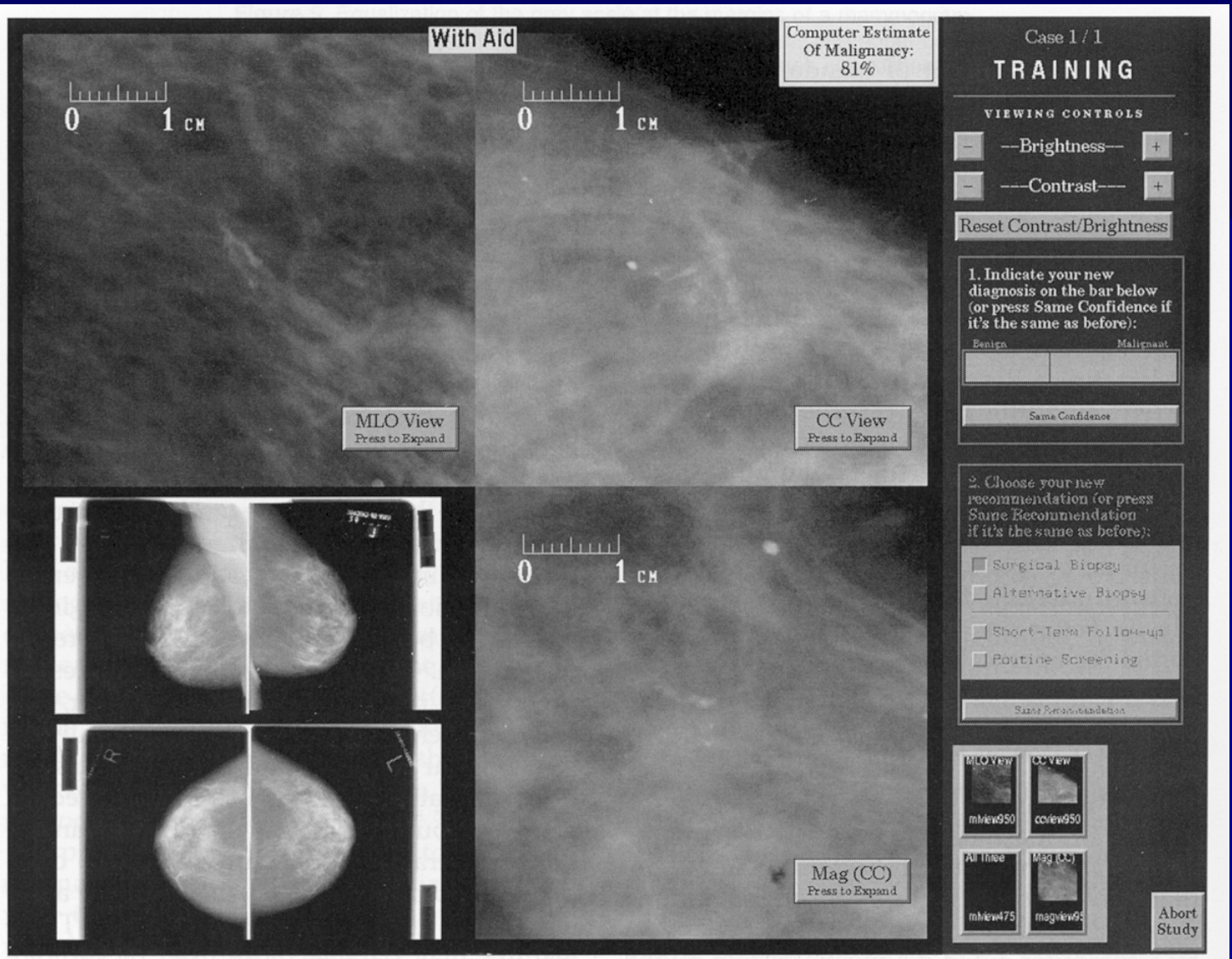


Figure 7. Display to convey computer diagnostic information to the radiologist. The computer estimated probability of malignancy for the lesion under study is 81%. A similar arrangement might be used for teaching purposes. (Courtesy of Y. Jiang, PhD, Chicago, IL.)

CAD workstation

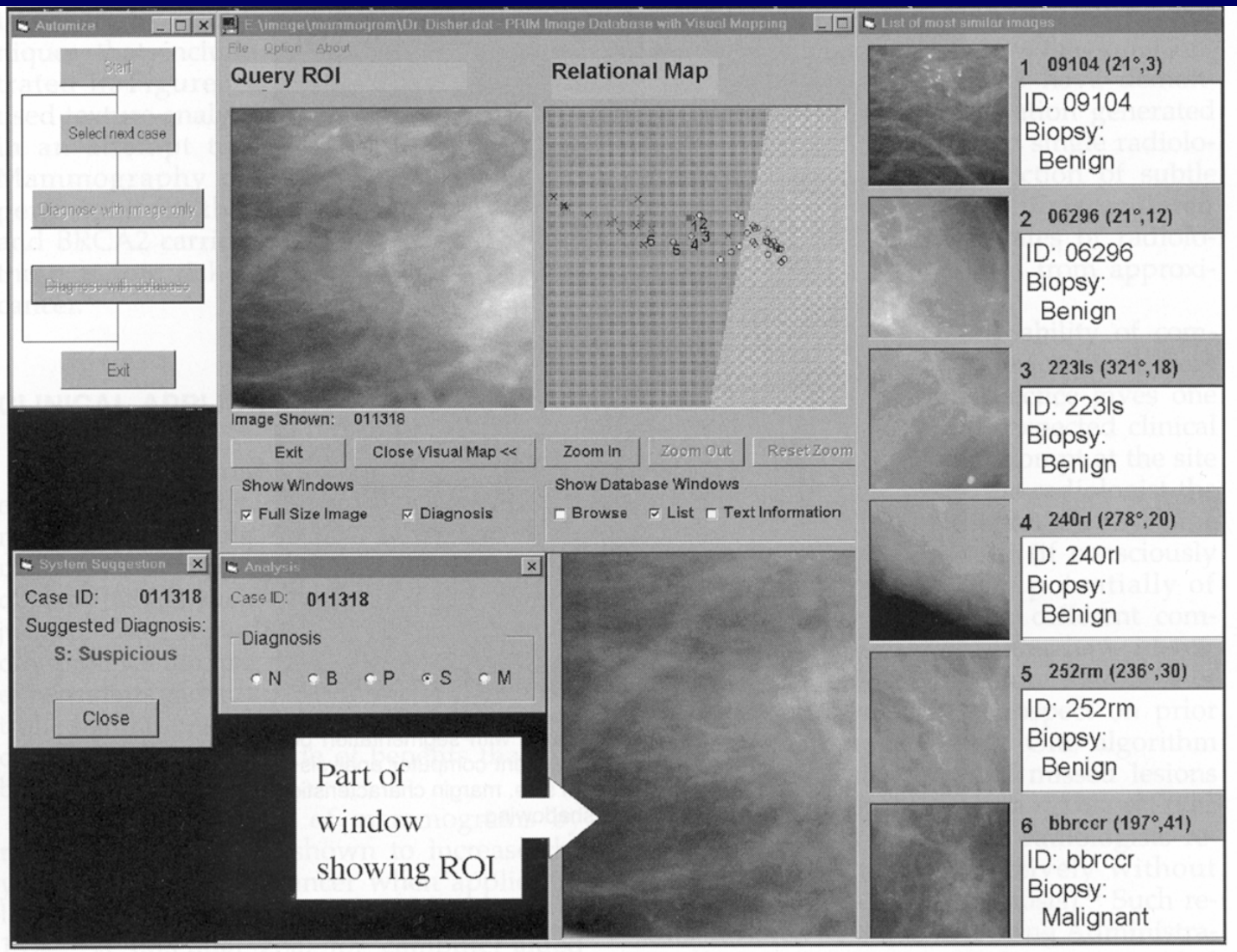


Figure 8. A second approach to present computer diagnostic information to the radiologist. Clusters of microcalcifications having characteristics similar to the one at hand are displayed in the small boxes at the right hand margin of the display. In this case, all but one displayed calcification clusters are benign. (Courtesy of J. Sklansky, Eng ScD, Los Angeles, CA.)